Assistant Secretary for Health
Office of Public Health and Science
Washington, DC 20201

Date: February 10, 2005

From: Deputy Assistant Secretary for Population Affairs

Subject: OPA Program Instruction Series, OPA 05-01:
Updated Safety Information for Depo-Provera Contraceptive Injection
(medroxyprogesterone acetate injectable suspension)

To: Regional Health Administrators, Regions I-X

On November 17, 2004, the U.S. Food and Drug Administration (FDA) announced that a "black box" warning would be added to the labeling of Depo-Provera Contraceptive Injection. This warning highlights that prolonged use of Depo-Provera may result in significant loss of bone density. The loss of bone density is greater the longer the drug is administered and may not be completely reversible after discontinuation of the drug. The "black box" warning indicates that Depo-Provera Contraceptive Injection should be used as a long-term birth control method (e.g., longer than two years) only if all other methods are inadequate. In addition, the warning states that it is unknown if the use of Depo-Provera Contraceptive Injection during adolescence or early adulthood will reduce peak bone mass and increase the risk of osteoporotic fracture in later life. On November 18, 2004, U.S. Pharmaceuticals, Pfizer Inc., the pharmaceutical company that manufactures Depo-Provera, issued letters to Healthcare Professionals and Healthcare Organization Leaders, informing them of the new "black box" warning, as well as other updated safety information included in the drug's labeling (copies of these letters are attached).

Although the FDA has indicated that Depo-Provera remains a safe and effective contraceptive (see attached "FDA Talk Paper"), the "black box" warning was added to the drug's labeling to "ensure that physicians and patients have access to this important information." The addition of the "black box" warning came as a result of the FDA's and Pfizer's analysis of data from two separate studies that showed Depo-Provera's effect on bone density during prolonged use. One study began in 1994 and enrolled 540 women ages 25 to 38. The other study--which started in 1997 and will continue through 2006--enrolled approximately 400 girls ages 12 to 18 who were taking the drug and is examining ways to reverse bone mineral density loss. References for these two studies are attached.

Depo-Provera has been authorized for use in Title X-funded projects since October 29, 1992, when the FDA announced approval of Depo-Provera for the prevention of pregnancy. Among females who received services in Title X-funded clinics during calendar year 2003, the Family Planning Annual Report (FPAR) reflected that 16 percent relied on Depo-Provera as their primary method of contraception.

As with other prescriptive contraceptive methods, Title X providers should ensure that medical protocols are developed and followed in accordance with the most current evidence-based information, accepted standards of care, and current recommendations for use. Title X providers should ensure that their medical protocols, informed consent and practice related to the use of Depo-Provera Contraceptive Injection are consistent with the November 17, 2004, "black box" warning added to the Depo-Provera package insert. Special consideration should be given to the potential impact of long term use in adolescence and early adulthood. It is incumbent on grantee agencies to ensure that delegate agencies and clinics have and use protocols that reflect this updated safety information.

If you have any questions, please contact Susan Moskosky, Director of the Office of Family Planning, on 301-594-4008.

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Attachments:

1) Depo-Provera Contraceptive Injection package insert, Revised November 2004.

2) "Dear Healthcare Professional Letter" and "Dear Healthcare Organization Leader Letter" from U.S. Pharmaceuticals Pfizer Inc, dated November 18, 2004.

3) FDA Talk Paper, November 17, 2004.

4) Requested Medical Information from Pfizer Inc., December 09, 2004. This information contains a summary of 29 studies and a review of 2 unpublished studies (includes references for the two studies cited in the Program Instruction).

cc: Regional Program Consultants
Regions I-X